OBSERVATIONS ON THE CARDIOVASCULAR SYSTEM IN THYROID DISEASE*

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The changes produced in the cardiovascular system by thyroid disease have long been appreciated by clinicians. There is need, however, to review some of the more important features observed, so that patients with grave cardiac disorders will not be subjected to unnecessary risk at operation nor will they be denied adequate treatment to support and restore the circulation.

It is our purpose to call attention to some irregularities of the heart in thyroid disease which are extremely common and which are not emphasized sufficiently in the literature. These irregularities play a considerable part in determining the outcome of the more severe cases and their recognition is not difficult.

The studies on which this report is based have been carried on at the University of California during the past two years.

GENERAL CONSIDERATIONS

Of the one hundred and eighty-one goiters studied, one hundred and twenty-three were classified as adenomas and fifty-eight as hyperplasias. In reviewing the adenomas, no attempt has been made to draw a sharp distinction between the toxic and non-toxic types. Approximately half of these cases showed no signs of toxicity and in a relatively small number the goiter produced pressure symptoms only. The average age was forty-six years and a tumor was noted at the average age of twenty-nine years, or seventeen years before appearing for treatment. Symptoms had been present on the average for eight and three-tenths years. Females were affected one hundred and six times and males seventeen times. Cardiovascular symptoms were more or less marked in forty-four per cent of the cases. Rapid and forceful beating of the heart and "palpitation" were the symptoms usually complained of, although vasomotor disturbances, irregularities of the heart, dyspnoea and breathlessness were frequently noted. Pain in the region of the heart and anginal attacks were rare. Central nervous system symptoms, including nervousness, tremors, astasia abasia and emotional instability were described in fifty-eight cases. Gastrointestinal symptoms, usually diarrhoea or diarrhoea alternating with constipation, were complained of in only four cases. There was marked progressive loss of weight in eight cases and a gain in two cases. In no case was there marked exopthalmos. When the eye changes were noted, usually only one or two of the minor signs were described. The average basal metabolic rate, when determined, was 30.2 per cent above the theoretical normal, but when the non-toxic cases were excluded, the average rate was 47 per cent above the theoretical normal. There were two deaths.

Of the fifty-eight cases with hyperplasia, forty-four presented exophthalmos and other eye signs and in five others these eye signs were slight or doubtful. The average age was thirty-six and four-tenths years and the tumor was observed at the average age of thirty-three and nine-tenths years, or two and five-tenths years before entering the hospital for treatment. Females were affected forty-three times and males fifteen times. Symptoms had been present for a relatively brief period. In about one-third of the cases, the tumor was noticed before the onset of symptoms; in about one-third the appearance of the symptoms preceded the discovery of the tumor; and in the remainder the symptoms and tumor appeared at the same time. The average duration of symptoms was about three months. Cardiovascular symptoms were complained of in 91 per cent of the cases. "Palpitation" and rapid, forceful beating of the heart were usually present; irregularities, dyspnoea, breathlessness and vaso-motor disturbances were common. Fifteen cases presented signs of decompensation. Central nervous system symptoms were present in fifty-six cases and were more pronounced than with the adenomas. Gastrointestinal symptoms such as diarrhoea and vomiting were complained of in seventeen cases. There was a definite loss of weight in thirty-eight cases. The basal metabolic rate averaged 58.7 per cent above the theoretical normal. There were seven deaths.

SPECIAL CONSIDERATIONS OF THE CARDIOVASCULAR SYSTEM

Symptoms—A brief statement of the cardiovascular symptoms is given above. It is the prevailing opinion that the hyperplastic goiter causes more profound changes in the circulatory system than is found in association with toxic adenomas. Our observations suggest, however, that, so far as the heart is concerned, the disturbances are practically the same in both groups. Where differences occurred, they seemed to be due mainly to the degree of toxicity. The vascular system, however, showed more pronounced changes in the hyperplastic group than in the group of adenomas. Among the earliest symptoms were tachycardia and a consciousness of the heart beat. Many patients complained of attacks of "palpitation." These spells, which were more frequent later in the disease, probably represent paroxysmal attacks of auricular fibrillation or flutter. Throbbing of the vessels in the neck and periphery, pulsation in the thyroid and a heaving precordium were usually marked in severe cases. Sleep was frequently interfered with because of these sensations and such patients preferred to lie on the right side. Dyspnoea and breathlessness on exertion, and in the later stages cough, progressive edema, cyanosis and other signs of decompensation were observed where proper treatment had not been instituted. Goiters producing pressure symptoms were relatively infrequent causes of cardiovascular disturbances as compared with the overacting glands.

Physical Signs—Inspection in the early cases revealed very little aside from a forceful apex impulse in the usual position, slightly increased carotid pulsations and flushing of the face and neck. As the disease advanced, the apex impulse

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(Most of the patients were on the surgical service of Dr. W. I. Terry, to whom we are indebted for the opportunity of making the studies here reported.)

became more forceful with a diffuse heaving of the precordium. The apex impulse was then displaced to the left and, in later stages, downward. The carotid arteries and peripheral vessels showed increased pulsations, and capillary pulsation was frequently noted, especially in the hyperplastic cases. When the myocardium began to fail, the venous pressure rose, the veins stood out and they occasionally showed unusual systolitic pulsations extending to the lower arm and hand (noted in three of our cases). When decompensation began, the usual signs appeared: such as pulsating liver, systolic venous pulse in the neck, edema of the lungs and edema of the legs advancing to anasarca. During the stage of decompensation, the heart was frequently irregular and no sign of an A-wave could be found in records from the jugular vein. On palpation the apex impulse was usually forceful and showed no displacement in early cases; but as the condition advanced, the impulse became more marked and diffuse, and it moved to the left and downward. A systolic or presystolic thrill at the apex, or a systolic thrill at the pulmonic area was noted in a few cases. A distinct shock was felt at the pulmonic area, accompanying the second sound. A systolic thrill was frequently felt over the thyroid vessels in hyperplastic glands, rarely in adenomas. The pulse was usually soft and oftentimes dichrotic. A water-hammer pulse was common in the hyperplasias. The rate was quickened in toxic cases, being ninety-three in the toxic adenomas and one hundred and seven in the hyperplasias in our series. In the early stages the pulse was generally regular, although a sinus arrythmia of the respiratory type was frequently observed. Later, many cases showed the more unusual types of irregularities, and in the terminal stages they were very commonly observed. By percussion the heart was found to be gradually enlarged to the left and downward, there was a well defined increase in dulness in the third and fourth left interspaces, as is seen in organic mitral disease, and later the dulness was increased to the right. Enlargement, usually to the left, was noted in forty-one of the adenomas and in forty-three hyperplasias. In the absence of thymic enlargement or a substernal extension of the thyroid, the substernal dulness was found to be increased, due to the dilatation of the great vessels. Auscultation revealed the signs of an overacting heart in toxic cases. The sounds were quickened, ringing and loud, giving an impression of hurried ineffectiveness. As the condition advanced, a soft systolic murmur was usually heard at the apex and a short, rough systolic murmur at the pulmonic area. Later a loud systolic murmur was frequently heard all over the precordium and was transmitted to the vessels of the neck, with a bruit over the thyroid vessels and gland. A definite bruit was noted over the gland in thirty-three of our cases of hyperplastic thyroids and in only three of the cases with adenomas. In the advanced stages of myocardial failure a diastolic murmur was occasionally heard at the pulmonic area or a soft systolic murmur appeared over the tricuspid area. Murmurs were noted in our series in forty-three cases of adenomas and in forty-six cases of hyperplasia.

An unusually large number of cardiac irregularities were observed. Of sinus arrhythmia we have no accurate data, as its finding was considered of little significance. It was frequently observed and possibly should be further studied. Extrasystoles were observed in only nine cases and in two of these it is probable that an unrecognized auricular fibrillation was present. Auricular fibrillation was observed in twenty-nine cases, occurring in nine cases with adenomas and twenty cases with hyperplasia. In fifteen of the twenty-nine cases the fibrillation was paroxysmal in type and in several cases many attacks were observed. In eight cases auricular fibrillation alternated with auricular flutter, and in two cases auricular flutter was observed alone. Paroxysmal auricular tachycardia with a rate of one hundred and ninety occurred in one case. (See Table 3.)

These observations on the frequency of cardiac irregularities have suggested that many of the attacks of "palpitation" which patients describe are due to a disturbance of the normal mechanism of the heart beat by the inception of one of these unusual rhythms. Such attacks frequently came on suddenly and usually lasted only a short time. They were accompanied by a sense of fulness in the chest, a disagreeable, rapid, forceful action of the heart, flushing of the face and neck, and breathlessness. The termination was usually abrupt.

On questioning patients who were seen during attacks of auricular fibrillation of flutter, it was found that their sensations were the same as those experienced during the previous spells of so-called palpitation. In our opinion this shows pretty clearly that what they call palpitation is really the result of serious auricular fibrillation or flutter. We feel sure that this has not been sufficiently recognized in the past.

X-ray studies on the toxic cases generally showed the heart to be enlarged to the left with widening in the region of the conus and left auricle—the so-called "mitral type." In some cases, particularly of the hyperplastic group, the heart was of the "aortic type" with the great-vessel shadow definitely increased.

Blood-pressure determination showed in the adenomas an average of 133 mm. Hg. (systolic), 78 mm. Hg. (diastolic) and a pulse pressure of 55 mm. Hg., while in the hyperplasias the average was 141 mm. Hg. (systolic) and 71 mm. Hg. (disastolic) with a pulse pressure of 70 mm. Hg. In several cases where the systolic and diastolic pressures were high before operation, a marked fall was observed following surgical treatment. Some of the more striking examples are shown in Tables 4 and 5. In one patient with a hyperplastic goiter who had a blood pressure of 200/100 on admission, there was a fall to 178/65 after medical treatment.

Venous Pressures and Pulsations—No attempt was made to measure accurately the venous pressures, but in advanced cases the pressure in the veins was definitely increased. In three cases we observed pulsating peripheral veins in the arms and hands, which cleared up after treatment.

Electrocardiagraph and Polygraph tracings were made on most of the cases showing unusual ir-

TABLE 1

General Findings

Type of goiter.....	No. of cases.....	Sex	Average age	Average age tumor noted	Average duration of symptoms	No. with eye signs.	No. with C. N. S. symptoms	No. with gastro-intestinal symptoms	Marked loss of weight	Average basal metabolism	No. of deaths.....
Adenomas toxic and non-toxic	123	M. 17 F. 106	41.38 yrs.	29.2 yrs.	8.3 yrs.	1 slight 6 doubtful	58	4	8	30.2% plus (all forms) 47% plus (toxic only)	2
Hyperplasias	58	M. 15 F. 43	36.4 yrs.	33.9 yrs.	3 mos.	44 5 doubtful	56	17	38	58.7% plus	7

TABLE 2

General Cardiovascular Findings

Type of goiter.....	No. of cases.....	Cardiac symptoms.	Per cent with cardiac symptoms...	Average pulse rate.	Average Blood pressure mm. Hg. Systolic	Average Blood pressure mm. Hg. Diastolic	Average pulse pressure mm. Hg.	No. with cardiac enlargement	No. with murmurs.	No. with bruit over thyroid or T. arteries	No. with signs of decompensation ..
Adenomas toxic and non-toxic	123	54	44%	85 (95 in toxic cases)	133	78	55	41	43	3	3
Hyperplasias	58	53	91%	107	141	71	70	43	46	33	15*

* Three of these cases presented unusual and marked systolic pulsations of the veins of the forearms and hands.

TABLE 3

Cardiac Irregularities

Type of Goiter	No. of Cases	Auricular Fibrillation	Auricular Flutter	Paroxysmal Tachycardia	Extra-systoles	Sinus Arrhythmia
Adenomas toxic and non-toxic	123	9 (4 paroxysmal) (2 alternating with auricular flutter)	3 and 1 probable (2 alternating with auricular fibrillation)	1 (rate 190)	6, including 2 cases of probable auricular fibrillation	Frequent No exact data
Hyperplasias	58	20 (11 paroxysmal) (6 alternating with auricular flutter)	4 and 2 probable (all alternating with auricular fibrillation)	0	3	Frequent No exact data
Totals	181	29	7 3 probable	1	7 2 doubtful	Frequent

TABLE 4

TOXIC ADENOMAS

Blood Pressure, mm. Hg.

Case No.	Before Operation	After Operation	Six Months Later
11447	215/105	140/80	170/90
12349	190/100	140/70	
12778	160/80	128/75	
13489	150/80	124/60	
11755	188/100	133/70	
13828	190/95	130/70	
13451	180/110	145/90	
8541	190/100	160/80	
10757	238/142	160/100	

TABLE 5

HYPERPLASIAS

Blood Pressure, mm. Hg.

Case No.	Before Operation	After Operation
12976	152/86	122/82
11586	145/65	138/45
10444	140/90	128/75

regularities and on some of the uncomplicated cases. Twenty-five cases were studied at intervals during their stay in the hospital. In addition to the changes in rhythm noted, there were certain variations in the auricular complex which were frequently observed in more severe cases. The P-waves were widened and increased in amplitude, frequently slightly notched in Lead I and having a diphasic character in Lead III. These features were noted in ten out of fourteen cases with regular rhythm. The P-R interval was 5/25 seconds in three cases and there was an arborization block in one case. Bundle branch lesions were not observed. Right hypertrophy was shown in two cases and left hypertrophy in three cases. The T-wave, when flattened or inverted in Leads I and II, has been found to indicate a bad prognosis in accordance with the findings of Krumbhaar. In our series there were six of such cases, all showing advanced myocardial disease and, as was to be expected, two or thirty-three per cent of them died.

Diagnosis—The diagnosis of the types of goiter studied were made on the clinical signs and symptoms combined with pathological findings at operation and necropsy. The cardiac symptoms and signs were usually obvious, although careful observation and instrumental means were frequently necessary to differentiate the irregularities encountered.

Treatment—No preliminary treatment was given in the non-toxic or moderately toxic adenomas previous to operation. The patients with more advanced toxic adenomas, with signs of cardiac failure, and many of the patients with hyperplasias were given preliminary medical treatment or received medical treatment alone. Mental and physical rest was insisted upon. Bromides or quinine hydrobromate were given when indicated. Ice bags were used over the thyroid gland and heart in the more toxic cases with considerable relief from distressing symptoms. Digitalis in the form of tincture was used, when indicated, under careful supervision. In moderate doses the drug produced excellent results and was very useful in controlling and possibly in preventing attacks of abnormal cardiac rhythms, particularly auricular fibrillation. One patient died during operation, possibly from the effects of excessive digitalization with "ventricular standstill." Another death occurred from auricular fibrillation with marked signs of thyrotoxicosis developing two days after operation. Quinidin sulphate seemed to have a beneficial effect in controlling attacks of auricular fibrillation in one case, although of no great benefit in several others. Cardiac decompensation has been treated by the approved methods, although excessive purgation has been very exhausting in some cases. X-ray treatment was used in many cases of hyperplasia before operation and in a few was the only local treatment employed. Radium emanations in bare tubes of 6-10 mc. were inserted into some of the more serious hyperplastic goiters with marked improvement. (These cases are being reported elsewhere by Dr. W. I. Terry.) Various methods of surgical treatment were employed, including ligation, enucleation of adenomata, partial lobectomy, bilateral subtotal lobectomy, etc.

One of the most striking observations made in this series of cases has been the degree of cardiac relief noted by the patient after removal of an overacting thyroid gland.

Prognosis—In our series it has been demonstrated that the condition of the heart generally determined the outcome of the case. Deaths from other causes, except marked increase of toxicity following operation in severe cases, were rare. Electrocardiographic demonstration of flattened or inverted T-waves in Leads I and II have indicated an unfavorable outcome. Heart block and disorders of the cardiac rhythm have been noted in the more severe cases. Signs of decompensation and advancing edema have indicated prolonged medical treatment or radio-therapy. Embolism and coronary disease were rare. Focal necroses of the liver and pancreas followed operation in one case and caused the death of the patient.

Mortality—In our series there were nine deaths, seven occurring in cases with hyperplasia, one with a mixed gland and one with an adenoma of the plunging type. In six of the nine cases death would be attributed to cardiac disease. In one of these there was embolism of the right subclavian artery. One patient had frequent attacks of angina pectoris and paroxysms of auricular fibrillation. In four cases auricular fibrillation was present at some time while under observation. Three cases presented unusual liver findings at necropsy and will be reported elsewhere at a later date. Two of the patients received medical treatment only.

CONCLUSIONS

The cardiovascular changes in thyroid disease are progressive, and in the most severe cases dominate the clinical picture.

The cardiac signs and symptoms in toxic adenomas and hyperplasias differ only with the degree of toxicity. The vascular changes are more marked in the cases of hyperplastic goiter.

Cardiac irregularities are more common than is generally recognized. Auricular fibrillation or auricular flutter, usually paroxysmal in type, occurred in about a third of all toxic cases. We believe that such paroxysmal attacks explain the periods of palpitation which are described by a large percentage of patients.

The prognosis depends in a large measure upon the condition of the circulation. If surgical treatment is to be carried out, the "time and extent of the operation should be governed by the circulatory condition."

Treatment of the thyroid heart depends on the stage of the disease. In all cases every measure should be employed to relieve the myocardium. Rest is essential. Sedative drugs are of some value. Elimination should be kept up. Digitalis is of great value in controlling auricular fibrillation and may be of value in preventing paroxysmal attacks. The amount required in controlling auricular fibrillation is usually less than in ordinary cardiac cases. It should be continued over long periods. Decompensation should be treated as in other myocardial cases.

The electrocardiogram is of value in recognizing myocardial changes in differentiating the types of irregularities and in prognosis.